

CLAIMS

What is claimed is:

1. A method for inhibiting the *in vitro* expression of a protein in a cell comprising contacting a cell with an oligomer, such that protein expression in the cell is inhibited, wherein said oligomer comprises an RNase H activating region and at least one nonactivating region, wherein at least one nonactivating region of the oligomer comprises at least one nucleomonomer having a 2' OH propargyl group.

2. The method of claim 1, wherein said oligomer further comprises 5' and 3' termini which are stabilized against exonucleases.

3. The method of claim 1, wherein the oligomer is about 15-40 nucleomonomers in length.

4. A method for inhibiting the *in vitro* expression of a protein in a cell comprising contacting a cell with a chimeric antisense oligomer, such that protein expression in the cell is inhibited, wherein said chimeric antisense oligomer comprises a 5' terminus; a 3' terminus; and 5'→3' linked nucleomonomers independently selected from the group consisting of 2'-modified phosphodiester linked nucleomonomers, and 2'-modified P-alkyloxyphosphotriester linked nucleomonomers; and wherein said 5' terminal nucleomonomer is attached to an RNase H activating region of between about three and ten contiguous phosphorothioate-linked nucleomonomers comprising deoxyribose, and wherein the 3' terminus of said oligonucleotide is selected from the group consisting of an inverted nucleomonomers, a contiguous stretch of about one to three phosphorothioate 2'-modified nucleomonomers, a biotin group, and a P-alkyloxyphosphotriester linked nucleomonomer, said oligomer having at least one nucleomonomer comprising a 2' OH propargyl group.

5. A method for inhibiting the *in vitro* expression of a protein in a cell comprising contacting a cell with a chimeric antisense oligomer, such that protein expression in the cell is inhibited, wherein said chimeric antisense oligomer comprises a 5' terminus; a 3' terminus; and 5'→3' linked nucleomonomers independently selected from the group consisting of 2'-

modified phosphodiester linked nucleomonomers and 2'-modified P-alkyloxyphosphotriester linked nucleomonomers; and wherein said 3' terminal nucleomonomer is attached to an RNase H-activating region of between about three and ten contiguous phosphorothioate-linked nucleomonomers comprising deoxyribose, and wherein the 5' terminus of said oligonucleotide is selected from the group consisting of an inverted nucleomonomer, a contiguous stretch of about one to three phosphorothioate linked 2'-modified nucleomonomers, a biotin group, and a P-alkyloxyphosphotriester nucleomonomer, said oligomer having at least one nucleomonomer comprising a 2' OH propargyl group.

6. A method for inhibiting the *in vitro* expression of a protein in a cell comprising contacting a cell with a chimeric oligomer, such that protein expression in the cell is inhibited, wherein said chimeric oligomer comprises a 5' terminus and a 3' terminus, an RNase H activating region, and at least one nonactivating region, wherein at least one nonactivating region comprises at least one unmodified RNA ribonucleotide selected from the group consisting of adenosine and guanine.

7. A method for inhibiting the *in vitro* expression of a protein in a cell comprising contacting a cell with a chimeric oligomer, such that protein expression in the cell is inhibited, wherein said chimeric oligomer comprises a 5' terminus and a 3' terminus, an RNase H activating region, and at least one nonactivating region, wherein at least one nonactivating region comprises a stretch of between about 5 and about 10 contiguous unmodified RNA ribonucleotides selected from the group consisting of adenosine and guanine.

8. A method for inhibiting the *in vitro* expression of a protein in a cell comprising contacting a cell with a chimeric antisense oligomer, such that protein expression in the cell is inhibited, wherein said chimeric antisense oligomer comprises a 5' terminus; a 3' terminus; and 5'→3' linked nucleomonomers independently selected from the group consisting of 2'-modified phosphodiester linked nucleomonomers; and 2'-modified P-alkyloxyphosphotriester linked nucleomonomers; and wherein said 5' terminal nucleomonomer is attached to an RNase H activating region of between about three and ten contiguous phosphorothioate-linked nucleomonomers comprising deoxyribose, and wherein the 3' terminus of said oligonucleotide is selected from the group consisting of an inverted nucleomonomer, a contiguous stretch of about one to three phosphorothioate linked 2'-modified

nucleomonomers, a biotin group, and a P-alkyloxyphosphotriester linked nucleomonomer said oligomer comprising a stretch of contiguous unmodified RNA nucleomonomers selected from the group consisting of adenosine and guanine.

9. A method for inhibiting the *in vitro* expression of a protein in a cell comprising contacting a cell with a chimeric antisense oligomer, such that protein expression in the cell is inhibited, wherein said chimeric antisense oligomer comprises a 5' terminus; a 3' terminus; and 5'→3' linked nucleomonomers independently selected from the group consisting of 2'-modified phosphodiester linked nucleomonomers, and 2'-modified P-alkyloxyphosphotriester linked nucleomonomers; and wherein said 3' terminal nucleomonomer is attached to an RNase H-activating region of between about three and ten contiguous phosphorothioate-linked nucleomonomers comprising deoxyribose, and wherein the 5' terminus of said oligonucleotide is selected from the group consisting of an inverted nucleomonomer, a contiguous stretch of about one to three phosphorothioate linked 2'-modified nucleomonomers, a biotin group, and a P-alkyloxyphosphotriester linked nucleomonomer said oligomer comprising a stretch of contiguous unmodified RNA nucleomonomers selected from the group consisting of adenosine and guanine.

10. A method for inhibiting the *in vitro* expression of a protein in a cell comprising contacting a cell with an oligomer, such that protein expression in the cell is inhibited, wherein said oligomer comprises an RNase H activating region, at least one nonactivating region, and at least one affinity enhancing agent, wherein said affinity enhancing agent is not positioned adjacent to the RNase H activating region.

11. A method for inhibiting the *in vitro* expression of a protein in a cell comprising contacting a cell with an chimeric antisense oligomer, such that protein expression in the cell is inhibited, wherein said chimeric antisense oligomer comprises a 5' terminus; a 3' terminus; and 5'→3' linked nucleomonomers independently selected from the group consisting of 2'-modified phosphodiester linked nucleomonomers and 2'-modified P-alkyloxyphosphotriester linked nucleomonomers; and wherein said 5' terminal nucleomonomer is attached to an RNase H activating region of between about three and ten contiguous phosphorothioate-linked nucleomonomers comprising deoxyribose, and wherein the 3' terminus of said oligonucleotide is selected from the group consisting of an inverted nucleomonomer, a contiguous stretch of one to three phosphorothioate linked 2'-modified

nucleomonomers, a biotin group, and a P-alkyloxyphosphotriester linked nucleomonomer, said oligomer comprising at least one affinity enhancing agent, wherein said affinity enhancing agent is not positioned adjacent to the RNase H activating region.

12. A method for inhibiting the *in vitro* expression of a protein in a cell comprising contacting a cell with a chimeric antisense oligomer, such that protein expression in the cell is inhibited, wherein said chimeric antisense oligomer comprises a 5' terminus; a 3' terminus; and 5'→3' linked nucleomonomers independently selected from the group consisting of 2'-modified phosphodiester linked nucleomonomers and 2'-modified P-alkyloxyphosphotriester linked nucleomonomers; and wherein said 3' terminal nucleomonomer is attached to an RNase H activating region of between about three and ten contiguous phosphorothioate-linked nucleomonomers comprising deoxyribose, and wherein the 5' terminus of said oligonucleotide is selected from the group consisting of an inverted nucleomonomer, a contiguous stretch of about one to three phosphorothioate linked 2'-modified nucleomonomers, a biotin group, and a P-alkyloxyphosphotriester linked nucleomonomer, said oligomer comprising at least one affinity enhancing agent, wherein said affinity enhancing agent is not positioned adjacent to the RNase H activating region.

13. The method of any of claims 1, 7, or 10, wherein said oligomer is linked to a transporting peptide.

14. The method of claim 13, wherein the transporting peptide comprises a peptide selected from the group consisting of an active portion of the antennapedia protein, an active portion of the transportan protein, and an active portion of the HIV TAT protein.

15. The method of any of claims 1, 7, or 10, wherein said cell is also contacted with a cationic lipid for at least about three days such that an oligomer is delivered to a cell.

16. The method of any one of claims 1, 4, or 5, wherein the at least one nucleomonomer comprising a 2' OH propargyl group linked to at least one adjacent nucleomonomer by a phosphodiester linkage.

17. The method of claim 1, wherein the oligomer comprises a 3' blocking group.

18. The method of any one of claims 6-9, wherein the at least one unmodified RNA ribonucleotide is linked to at least one adjacent nucleomonomer by a phosphodiester linkage.